

Amendments to the Claims

The following listing of the claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) An isolated expression vector comprising (a) one or more silencer elements and one or more conditionally inducible elements to form a silencer-inducible region, and (b) a promoter in operative linkage with at least one silencer-inducible region, wherein said promoter is thereby regulated by said at least one silencer-inducible region, and said promoter is upstream of at least one nucleotide sequence; [said expression vector under an inducing condition expressing said at least one nucleotide sequence in an amount greater than expression of said at least one nucleotide sequence without said inducing condition] wherein at least one of said silencer elements and one of said conditionally inducible elements are arranged within 500 nucleotides of each other; and wherein silencing of expression of said at least one nucleotide sequence from said expression vector is reversed in the presence of an inducing condition.
2. (Withdrawn) The expression vector of claim 1, wherein said promoter is a viral promoter.
3. (Withdrawn) The expression vector of claim 1, wherein said promoter is a mammalian promoter active in a plurality of different tissues.

4. (Previously presented) The expression vector of claim 3, wherein said mammalian promoter is active in one or more tissues selected from the group consisting of cardiac muscle skeletal muscle, vascular endothelium, brain, retina, kidney, liver, lung, bone marrow and spleen.

5. (Original) The expression vector of claim 1, wherein said promoter is a cell-type specific promoter.

6. (Previously presented) The expression vector of claim 5, wherein said cell-type specific promoter is selected from the group consisting of a cardiac muscle-specific promoter, a skeletal muscle-specific promoter, an endothelial cell-specific promoter, a neuron-specific promoter, a glia-specific promoter, a retina-specific promoter, a kidney-specific promoter, a liver-specific promoter, a lung-specific promoter, a lymphocyte-specific promoter, a myeloid-specific promoter, and a tumor-specific promoter.

7. (Previously presented) The expression vector of claim 1, wherein at least one of said silencer elements is a neuron restrictive silencer (NRS) element to which neuron restrictive silencer (NRS) transcription factor binds.

8. (Original) The expression vector of claim 1, wherein at least one of said silencer elements is a negative regulatory element (NRE) or repressor.

9. (Previously presented) The expression vector of claim 1, wherein at least two of

said silencer elements are from genes selected from the group consisting of genes designated adenine nucleotide transporter-2, B29 (lg- β), CD95 (Fas/APO1), glutathione transferase P (GST-P), interferon- β (IFN- β), intestinal trefoil factor (ITF), lysozyme, metallothionein III (MT-III), testis specific histone H1t, thyroid hormone receptor- β 1 (TR- β 1), vascular cellular adhesion molecule-1 (VCAM-1), human synapsin, and von Willebrand factor (vWF).

10. (Withdrawn) The expression vector of claim 1, wherein at least two of said silencer elements are bound by transcription factors selected from the group consisting of CCTC binding factor (CTCF), goblet cell silencer inhibitor (SI), nuclear factor I (NFI) proteins, octamer binding proteins (Oct-1 and Oct-2), silencer factor A, and silencer factor B.

11. (Previously presented) The expression vector of claim 1, wherein at least one of said conditionally inducible elements is a hypoxia response enhancer (HRE) element to which hypoxia inducible factor-1 (HIF-1) transcription factor binds.

12. (Previously presented) The expression vector of claim 11, wherein said HRE element is from a gene selected from the group consisting of genes designated endothelin-1, enolase-1, erythropoietin, heme oxygenase, phosphoglycerate kinase, pyruvate kinase, and VEGF/FIt-1 receptor.

13. (Withdrawn) The expression vector of claim 1, wherein HIP- 1 a does not bind said HRE element.

14. (Withdrawn) The expression vector of claim 1, wherein at least one of said conditionally inducible elements is an oxidative stress response element.

15. (Withdrawn) The expression vector of claim 1, wherein at least one of said conditionally inducible elements is an anti-oxidant response element.

16. (Withdrawn) The expression vector of claim 1, wherein at least one of said conditionally inducible elements is selected from the group consisting of a metal response element (MRE), heat response element, a hormone response element, and growth factor response element.

17. (Withdrawn) The expression vector of claim 1, wherein at least one of said conditionally inducible elements is an NF- κ B responsive element to which NF- κ B transcription factor binds;

18. (Previously presented) The expression vector of claim 1, wherein said at least one nucleotide sequence is a functional coding region of a gene selected from the group consisting of adenosine deaminase, angiopoietin, apoptosis inhibitor protein, angiostatin, B-cell CLL/lymphoma (BCL2), catalase, deoxyribonuclease, DT-diaphorase, endostatin, erythropoietin, fibroblast growth factor (FGF), fumagillin, 13-globin, glutathione peroxidase, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), heat shock transcription factor, hepatocyte growth factor (HGF), interferon, tissue metalloproteinase inhibitor, nitric oxide synthase, platelet derived growth factor

(PDGF), proliferin, somatomedin C (IGF-15, superoxide dismutase, survivin, thymidine kinase, tissue plasminogen activator, tumor protein p53 (TP53), urokinase, and vascular endothelial growth factor (VEGF).

19. (Previously presented) The expression vector of claim 1, wherein said at least one nucleotide sequence is a functional coding region of a reporter gene selected from the group consisting of chloramphenicol transferase, green fluorescent protein, red fluorescent protein, β -galactosidase, β -glucuronidase, β -lactamase, and luciferase.

20. (Withdrawn) The expression vector of claim 1, wherein said at least one nucleotide sequence is a functional portion of a gene selected from the group consisting of MDM2, tumor protein p53 (TP53), endothelin-I, tumor necrosis factor (TNF), interleukin, interferon (IFN), and vascular endothelial growth factor (VEGF), and wherein said nucleotide sequence is positioned in the antisense orientation relative to said promoter.

21. (Previously presented) The expression vector of claim 1, wherein at least one silencer element and at least one conditionally inducible element are heterologous with respect to each other.

22. (Canceled)

23. (Previously presented) The expression vector of claim 1 which is a plasmid present in a formulation for introduction into a cell by a technique selected from the group

WPB:177570:1

consisting of electroporation, microinjection, and infusion.

24. (Original) The expression vector of claim 1 which is packaged as a replication defective adenovirus.

25. (Original) The expression vector of claim 1 which is packaged as an adeno-associated virus.

26. (Original) The expression vector of claim 1 which is packaged as a retrovirus.

27. (Original) The expression vector of claim 1 which is between 1000 and 50,000 nucleotides in length.

28-41 (Canceled)

42. (Previously presented) The expression vector of claim 1, wherein said expression vector contains one or more signals selected from the group consisting of a Kozak consensus sequence upstream of said nucleotide sequence, one or more mRNA degradation signals, a termination of transcription signal, a polyadenylation signal, and a 3' cleavage signal.

43. (Previously presented) The expression vector of claim 1, wherein at least one silencer element and one conditionally-inducible element are separated by no more than 50 nucleotides,

WPB:177570:1

44. (Previously presented) The expression vector of claim 1, wherein at least one silencer element and one conditionally-inducible element are separated by no more than 100 nucleotides.

45. (Previously presented) The expression vector of claim 1, wherein at least one silencer element and one conditionally-inducible element are separated by no more than 200 nucleotides.

46. (Previously presented) The expression vector of claim 1, wherein said expression vector comprises at least two different silencer elements.

47. (Previously presented) The expression vector of claim 1, wherein said expression vector comprises at least two different conditionally inducible elements.

48. (Previously presented) The expression vector of claim 1 wherein at least one of said silencer elements and at least one of said conditionally inducible elements overlap.

49. (Previously presented) The expression vector of claim 1, wherein said expression vector contains at least two of said silencer elements and at least two of said conditionally inducible elements, and wherein said silencer elements and said conditionally inducible elements alternate.

50. (Canceled) The expression vector of claim 1, wherein said expression vector contains at least two of said silencer elements and at least two of said conditionally inducible elements, and wherein said silencer elements and said conditionally inducible elements alternate.

51. (Previously presented) The vector of claim 1, wherein said silencer-inducible region is in the sense orientation with respect to said nucleotide sequence.

52. (Previously presented) The vector of claim 1, wherein said silencer-inducible region is in the antisense orientation with respect to said nucleotide sequence.

53. (Previously presented) An isolated expression vector comprising (a) one or more silencer elements and one or more conditionally inducible elements to form a silencer-inducible region, and (b) a promoter in operative linkage with at least one silencer-inducible region, wherein said promoter is thereby regulated by said at least one silencer-inducible region, and said promoter is upstream of a polylinker, said polylinker containing a plurality of restriction endonuclease recognition sites, wherein, when a nucleotide sequence is cloned into one of said restriction endonuclease recognition sites in said polylinker, said expression vector under an inducing condition expresses said nucleotide sequence in an amount greater than the expression of said at least one nucleotide sequence without said inducing condition.

54. (Withdrawn) The expression vector of claim 53, wherein said promoter is a viral promoter.

55. (Withdrawn) The expression vector of claim 53, wherein said promoter is a mammalian promoter active in a plurality of different tissues.

56. (Previously presented) The expression vector of claim 53, wherein at least one of said silencer elements is a neuron restrictive silencer (NRS) element to which neuron restrictive silencer (NRS) transcription factor binds.

57. (Previously presented) The expression vector of claim 53, wherein at least one of said silencer elements is a negative regulatory element (NRE) or repressor.

58. (Previously presented) The expression vector of claim 53, wherein at least one of said conditionally inducible elements is a hypoxia response enhancer (HIRE) element to which hypoxia inducible factor-1 (HIF-1) transcription factor binds.

59. (Withdrawn) The expression vector of claim 53, wherein at least one of said conditionally inducible elements is an NP-KB responsive element to which NP-KB transcription factor binds.

60. (Previously presented) The expression vector of claim 11, wherein the sequence of said HRE element is SEQ ID NO: 1.